

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0000055341	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/EP2004/008624	International filing date (<i>day/month/year</i>) 31.07.2004	Priority date (<i>day/month/year</i>) 18.08.2003
International Patent Classification (IPC) or national classification and IPC C12N15/82		
Applicant SUNGENE GMBH & CO. KGAA		

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>13</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																									
<p>4. This report contains indications relating to the following items:</p> <table> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input checked="" type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I

Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☐ the international application as originally filed/furnished
- ☒ the description:
- pages 1-76 _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- nos. 1-18 _____ as originally filed/furnished
- nos.* _____ as amended (together with any statement) under Article 19
- nos.* _____ received by this Authority on _____
- nos.* _____ received by this Authority on _____
- ☐ the drawings:
- sheets _____ as originally filed/furnished
- sheets* _____ received by this Authority on _____
- sheets* _____ received by this Authority on _____
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 1-3, 8-18 (in part), 5-7 (in full)

because:

- ☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 1-3, 8-18 (in part), 5-7 (in full)

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

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Box No. IV

Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:
 - ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ neither restricted the claims nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
 - ☐ complied with.
 - ☒ not complied with for the following reasons:

See Supplemental Box
4. Consequently, this report has been established in respect of the following parts of the international application:
 - ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-3, 8-18 (in part), 4 (in full)

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1.	Statement		
	Novelty (N)	Claims <u>4</u>	YES
		Claims <u>1-3, 8-18</u>	NO
	Inventive step (IS)	Claims <u>1-4, 8-18</u>	YES
		Claims <u>1-4, 8-18</u>	NO
	Industrial applicability (IA)	Claims <u>1-4, 8-18</u>	YES
		Claims <u>1-4, 8-18</u>	NO
2.	Citations and explanations (Rule 70.7)		
	Reference is made to the following documents:		
	D1: DE 102 53 112 A (SUNGENE GMBH & CO KGAA) 3 June 2004 (2004-06-03)		
	D2: BENFEY P N ET AL: "SEQUENCE REQUIREMENTS OF THE 5 ENOLPYRUVYL SHIKIMATE-3-PHOSPHATE SYNTHASE 5'-UPSTREAM REGION FOR TISSUE-SPECIFIC EXPRESSION IN FLOWERS AND SEEDLINGS" Plant Cell, Vol. 2, No. 9, 1990, pages 849-856, XP008040624		
	D3: WO 98/14465 A (COLORADO STATE UNIVERSITY THRO (US)) 9 April 1998 (1998-04-09)		
	D4: WO0066747 A (ZENECA LTD) 9 November 2000 (2000-11-09)		
	D5: WO 02/061050 A (UNIV MARYLAND) 8 August 2002 (2002-08-08).		
1.	Basis of the report		
	The applicant's attention is drawn to the fact that the present report is established with regard to the searched claims of invention 1 only.		

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
2.	Claimed priorities <p>The present application claims priorities of six international applications. These international applications in turn likewise claim different (national) priorities. Article 4 of the Paris Convention for the Protection of Industrial Property and PCT Article 8 state that a priority right for a particular subject matter can be claimed for a single period of 12 months. In the case of the present application this means that the subject matter of the older, national priorities no longer enjoys the (further) priority of the more recent six international applications claimed for the present application; in other words, the six international priorities claimed for the present application are taken into consideration only insofar as they do <u>not</u> relate to the subject matter of the different national priorities. It follows further that the overlapping contents of the different national priorities, insofar as it was published prior to the international filing date 31 July 2004, is considered the prior art with regard to the present application.</p>
3.	Novelty and inventive step (PCT Article 33(2) and (3))
3.1	The present application relates to the use of the EPSPS promoter for the expression of genes in plants of the genus <i>Tagetes</i> and genetically

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
	<p>modified <i>Tagetes</i> plants which either express an endogenous gene under the control of a heterologous EPSPS promoter or use the endogenous EPSPS promoter for the expression of a heterologous gene or a heterologous EPSPS promoter for the expression of a heterologous gene. Methods for the production of biosynthetic products such as, for example, carotenoids, by cultivation of these plants are likewise claimed.</p> <p>3.2 Document D1 (see Box V., point 1) discloses methods for the production of carotenoids in genetically modified organisms. The EPSPS promoter is suggested for the flower-specific expression of genes of the carotenoid synthesis pathway in <i>Tagetes</i> plants ([0174], [0135]-[0136]).</p> <p>The subject matter of claims 1-3 and 8-18 is therefore not novel with respect to D1 and the subject matter of claim 4 is not inventive, since the specific EPSPS sequences SEQ ID NO:1 and 2 are already known from document D2 (see the database entry AC: M37029; SEQ ID NO:1 and 2 are 100% identical to the sequence disclosed in M37029) and the EPSPS sequence SEQ ID NO: 3 is 98.65 % identical to the sequence known from document D2, without this sequence difference apparently being linked to a special technical effect.</p> <p>3.3 Document D3 describes the production of transgenic geraniums and roses which express ACC synthase antisense RNA, <i>inter alia</i> under the control of the</p>

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
	<p>EPSPS promoter (page 12, line 3, to page 13, line 12).</p> <p>3.4 Document D4 discloses a method for producing diverse herbicide-resistant plants. As part of this method it claims the use of an EPSPS promoter of rice in conjunction with an EPSPS-coding sequence, as well as transgenic plants comprising a corresponding vector (page 2, line 30, to page 3, line 16; page 7, lines 1-27). Various plants belonging to different genera are mentioned as preferred transgenic plants, the genus <i>Tagetes</i> not being expressly specified.</p> <p>Documents D3 and D4 indicate that the EPSPS promoter is used for gene expression in diverse plant genera. To a person skilled in the art it would therefore be obvious that, as long as there is no concrete information to the contrary, this promoter, which is known per se, is also suitable for gene expression in the genus <i>Tagetes</i>. The subject matter of claims 1-4 and 8-14 could be considered inventive only if the use of the EPSPS promoter in <i>Tagetes</i> has an unexpected effect or property relative to the use in other plant genera. However, the application does not specify effects or properties of this kind. Consequently, relative to documents D3 and D4 the subject matter of claims 1-4 and 8-14 appears to be concern merely a random selection among several parameters known to a person skilled in the art (here: special promoter and special host plant), and</p>

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
	<p>therefore cannot be considered inventive (PCT Article 33(3)).</p> <p>3.5 Document D5 mentions, <i>inter alia</i>, the use of flower-specific promoters for the production of carotenoids in <i>Tagetes</i> (page 18, line 13, to page 19, line 3). The EPSPS promoter is not expressly specified. However, since it is already known from documents D2 (and D1) that EPSPS is one of the flower-specific promoters, it would be obvious to a person skilled in the art to use the flower-specific EPSPS promoter for the production of carotenoids in <i>Tagetes</i>. Consequently, the subject matter of claims 1-4 and 8-18 is not inventive relative to documents D5 and D2 (PCT Article 33(3)).</p>

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
- a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:
- The sequence listing in the description, pages 1-171, as originally filed.

* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box IV

Unity of invention (PCT Article 3(4)(iii) and 17(3)(a))

The different inventions are:

- 1) Invention 1: claims 1-3 and 8-18 (in part) and claim 4 (in full)

The use of an EPSPS promoter, genetically modified plants of the genus *Tagetes*, and methods for producing biosynthetic products.

- 2) Invention 2: claims 1-3 and 8-18 (in part) and claim 5 (in full)

Use of a B-gene promoter, genetically modified plants of the genus *Tagetes*, and method for producing biosynthetic products.

- 3) Invention 3: claims 1-3 and 8-18 (in part) and claim 6 (in full)

Use of a PDS promoter, genetically modified plants of the genus *Tagetes*, and method for producing biosynthetic products.

Supplemental Box

- 4) Invention 4: claims 1-3 and 8-18 (in part) and claim 7 (in full)

Use of a CHRC promoter, genetically modified plants of the genus *Tagetes*, and method for producing biosynthetic products.

For the following reasons these inventions are not so linked as to form a single general inventive concept (PCT Rule 13.1):

The invention concerns the use of promoters for the flower-specific expression of genes in *Tagetes*, wherein the promoters are selected from the group consisting of EPSPS, B-gene, PDS and CHRC promoters.

Promoters which control the flower-specific expression of genes in *Tagetes* and transgenic *Tagetes* plants containing these vectors are already described in the prior art. For example, document WO 0032788 discloses the use of a flower-specific promoter for the expression of genes of the carotenoid pathway, in order to manipulate the carotenoid content of *Tagetes* flowers (page 8, lines 4-10; page 18, lines 12-29; page 22, line 30, to page 23, line 3). In addition, document EP0524910 discloses the use of a flower-specific promoter for the expression of genes in *Tagetes* (page 3, line 36, to page 4, line 13; page 4, lines 29-41).

In the light of the above prior art the problem to be solved by the present application is understood to be that of making available additional promoters which

Supplemental Box

control flower-specific gene expression in *Tagetes*. The promoters specified in inventions 1 to 4 correspond to different solutions to the above problem.

In view of the fact that promoters for the flower-specific expression of genes in *Tagetes* were already described in the prior art, and in the light of the absence of further technical features which might be considered special technical features, the international searching authority has arrived at the conclusion that the four claimed inventions of the present application are not linked by a single general inventive concept within the meaning of PCT Rule 13.1.

Consequently, the application does not meet the unity of invention requirement and the different inventions, which do not contain a shared inventive concept, were listed by contents as above (PCT Article 17(3)(a)).